REMARKS

Claims 1-4, 6-10, 12, 23-26, 28-29 and 34-37 are pending in the application. Claims 1 and 23 have been amended. Support for the amendments to the claims can be found throughout the originally filed specification and claims. Support for the amendments to claims 1 and 23, can be found, for example, at page 2, line 26 to page 3, line 4, and at page 4, lines 30-34. No new matter has been added.

The amendment to specification merely corrects a typographical error in the serial number of the priority application. (The correct serial number was presented on the application data sheet and already appears on the official filing receipt.)

Amendment of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and has been done solely to more particularly point out and distinctly claim the invention, to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Applicants' representative thanks Examiners Ford and Barnhart for the courtesy of an interview at the United States Patent and Trademark Office on December 6, 2007. During the interview, the pending claims and prior art were discussed. In light of the amendments and remarks presented herein and during the December 6, 2007 interview, Applicants believe claims the pending claims are now in condition for allowance, and respectfully request reconsideration and allowance..

Rejection of Claims 1-4, 6-10, 12, 23-26, 28-29 and 33 are rejected under 35 U.S.C. 103(a)

Claims 1-4, 6-10, 12, 23-26, 28-29 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naughton *et al* (US 2003/0007954), in view of Lu *et al.* (Circulation, 2001), Atala *et al.* (US Patent 6,479,064), MacLaughlin et al. (US Patent 6,692,738) and Penn et al (US 2004/0161412 A1, 60/405,274 and 60/424,065). Applicants traverse this rejection.

During the interview, Applicants' representative express the concern that an inordinately large number of disparate references – six references in total – were being combined to support the obviousness rejection. Applicants' representative asserted that reconstructing the claimed invention from a large number of prior art references by using the claim itself as a blueprint was not an appropriate basis for an obviousness determination.

It was also noted that some of the references actually taught away from the claimed invention. Penn, for example teaches transient expression of growth factors but not encapsulation. Springer, on the other hand, teaches encapsulation but not transient expression. No motivation can be found in either reference for the combination of both techniques to ensure the short-term stimulation of blood vessel growth for organ augmentation.

Even more telling was the fact that the Rinsch reference ("*Delivery of FGF-2 but not VEGF by encapsulated genetically modified myoblasts improves survival and vascularization in a model of acute skin flap ischemia*" Gene Therapy (2001) 8, 523-533) suggests that encapsulated VEGF-producing cells are not effective in promoting vascularization.

During the interview, it was noted that the use of encapsulation in the present invention allows nutrients to reach the transfected cells and permits the VEGF proteins secreted from the cells to diffuse into the surrounding tissues while protecting the transfected cells from the immune environment. The use of transient expression ensures that the induced angiogenesis is a short-term effect. Moreover, as further discussed on page 5 of Applicants' specification, the degree of VEGF secretion and the period of delivery can be regulated by modulating the number of engineered cells which are encapsulated per microsphere, as well as the number of microspheres injected. Thus, the claimed invention describes a method of transient and local VEGF administration to promote localized angiogenesis with minimal systemic side effects.

As discussed during the interview, and in order to expedite prosecution, Applicants have further amended independent claims 1 and 23 to clarify Applicant's contribution to the art.

As amended, independent claim 1 now recites the steps of *transiently* transfecting a first population of cells with a plasmid encoding for VEGF, such that said first population of cells express VEGF for *less than about 10 weeks*; *encapsulating the transfected cells*; selecting a second population of cells *to be assimilated at a target tissue region*, wherein the second population of cells comprises *myoblasts*; suspending the first population of cells and the second population of cells in an *injectable polymer matrix*; injecting both populations and the polymer matrix into the target tissue region where the first population of cells will express the VEGF and thereby induces assimilation and *differentiation of the myoblasts* in the target region and augmenting organ function.

Similarly, as amended, claim 23, now recites the steps of culturing at least a first population of cells on a matrix material to produce an organ construct; *transiently transfecting* a second population of cells with a plasmid encoding an angiogenesis modulating agent, wherein the second population of cells comprises cells of a different cell type than the first population, wherein either the first or second population of cells comprises myoblasts; *encapsulating the transfected cells*; and implanting the organ construct and the transfected cells *in vivo* at one target site to replace or augment organ function, such that the *transfected cells express the angiogenesis modulating agent for less than about 3 weeks* and the first population of cells assimilate and differentiate at the target site.

None of the cited references teach or suggest the invention as a whole, much less the benefits of encapsulating transiently transfected cells, such that the encapsulated transfected cells are protected from the immune system, while allowing the release of an angiogenesis modulating factor (See Page 3, lines 1-4 of Applicants' specification).

CONCLUSION

In summary, the above-identified patent application has been amended and reconsideration is respectfully requested for all the reasons set forth above. In the event that the amendments and remarks are not deemed to overcome the grounds for rejection, the Examiner is kindly requested to telephone the undersigned representative to discuss any remaining issues.

Respectfully submitted,

NUTTER McCLENNEN & FISH LLP

Date: December 28, 2007

Thomas J. Engellenner
Registration No.: 28,711
Attorney for Applicants
World Trade Center West
155 Seaport Boulevard
Boston, MA 02210-2604
Tel: (617) 439-2948
Fax: (617) 310-9948

1690606.1